

Sub
B1
1. A method for detecting the presence of a mammalian target nucleic acid which contributes to the etiology of a neoplasm, in a tissue specimen, wherein the specimen is external to a primary neoplasm and the specimen does not exhibit morphological characteristics indicative of neoplastic pathology, and the target nucleic acid is present in the primary neoplasm and the specimen, the specimen being selected from the group consisting of a tumor margin, a regional lymph node, the method comprising extracting the nucleic acid present in the specimen and detecting the presence of the target nucleic acid.

2. The method of claim 1, wherein the nucleic acid is amplified before detecting.

3. The method of claim 2, wherein the amplification is by means of oligonucleotides that hybridize to the flanking regions of the target nucleic acid.

4. The method of claim 1, wherein the target nucleic acid contains a mutation, a restriction fragment length polymorphism, a nucleic acid deletion, or a nucleic acid substitution, as compared with a corresponding wild-type nucleic acid in the specimen.

5. The method of claim 1, wherein the target nucleic acid is selected from the group consisting of an oncogene and a tumor suppressor gene.

6. The method of claim 5, wherein the tumor suppressor gene is selected from the group consisting of APC, DCC, NF1, NF2, Rb, RET, VHL, WT-1 and p53.

7. The method of claim 1, wherein the neoplasm is of the head.

8. The method of claim 1, wherein the neoplasm is of the neck.

9. The method of claim 1, wherein the neoplasm is benign.

10. ~~The method of claim 1, wherein the neoplasm is malignant.~~

11. The method of claim 2, wherein the amplified nucleic acid is cloned before detecting.

12. A method for detecting metastases in a subject having an excised tumor comprising:

- a) isolating tissue from a surgical margin or lymph node adjacent to said excised tumor;
- b) applying to said tissue an oligonucleotide that preferentially hybridizes to a neoplastic nucleic acid, and
- c) detecting the presence of said neoplastic nucleic acid, wherein the presence of said neoplastic nucleic acid indicates metastases.

13. The method according to claim 12 wherein no more than an average of about one out of every ten thousand cells of said tissue have a neoplastic nucleic acid.

14. The method according to claim 12 wherein said tissue appears normal under a microscope.

15. The method according to claim 12 wherein said neoplastic nucleic acid is a mutated tumor suppressor gene.

16. The method according to claim 15 wherein said tumor suppressor gene is the p53 gene.

Sub 432 17. ~~The method according to claim 12 wherein said neoplastic acid is an~~
oncogene

18. A method for detecting a mammalian target neoplastic nucleic acid in a tissue specimen which is external to a primary neoplasm, comprising extracting the nucleic acid present in the specimen and detecting the presence of the target nucleic acid.

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c3

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